

101



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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/075,521  | 02/14/2002  | Piyasena Hewawasam   | CT-2640-NP          | 8919             |
| 23914   | 7590        | 04/19/2004           | EXAMINER            |                  |
| STEPHEN B. DAVIS<br>BRISTOL-MYERS SQUIBB COMPANY<br>PATENT DEPARTMENT<br>P O BOX 4000<br>PRINCETON, NJ 08543-4000 |             |                      | JONES, DWAYNE C     |                  |
|   |             |                      | ART UNIT            | PAPER NUMBER     |
|   |             |                      | 1614                |                  |
| DATE MAILED: 04/19/2004   |             |                      |                     |                  |

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/075,521             | HEWAWASAM ET AL.    |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Dwayne C Jones         | 1614                |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 21 November 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,2,5 and 6 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,5 and 6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)     | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Status of Claims***

1. Claims 1, 2, 5, and 6 are pending.
2. Claims 1, 2, 5, and 6 are rejected.
3. Claims 3 and 4 were cancelled as per the amendment of November 21, 2003.

### ***Response to Arguments***

4. Applicants' arguments filed November 21, 2003 have been fully considered but they are not persuasive with respect to the rejections over Bos et al. as well as Suto et al. Applicants present the following arguments. First, applicants argue that Bos et al. do not teach of the instantly claimed compounds. Second, applicants argue that the compounds of Bos et al. are antagonists of NK-1 that are used to treat other ailments. Third, applicants allege that Suto et al. do not suggest the current intended use of the instant claims.

5. First, applicants argue that Bos et al. do not teach of the instantly claimed compounds and that the compounds of Bos et al. are antagonists of NK-1 that are used to treat other ailments. Bos et al. teach of the compounds of formula 1, wherein R<sup>5</sup> is lower alkyl, lower alkoxy, amino, and phenyl, which correspond to instant variable R<sup>2</sup>. Instant variable of R<sup>3</sup> can be hydrogen as in Bos et al. Instant variable of R<sup>1</sup> can be represented by phenyl as in Bos et al., especially when Bos et al. variable of R<sup>1</sup> is hydrogen, n is 0, and R<sup>2</sup> is hydrogen. When the variable of X is C(O)NR<sup>4</sup> and further where R<sup>4</sup> is hydrogen or lower alkyl, this group corresponds to instant variables R<sup>4</sup> or

Art Unit: 1614

R<sup>5</sup>. In addition, when the Bos et al. variables of R<sup>4</sup> and R<sup>4'</sup> are hydrogen and the variable of n is 0, the instant variables of R<sup>4</sup> and R<sup>5</sup> are clearly rendered obvious. It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the Bos et al. reference, including those of the claims, because an ordinary artisan would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as the genus as a whole.

6. Second, applicants further purport that the pharmaceutical compounds of Bos et al. have a different intended uses than the instant claims. However, it is first mentioned that instant claims 5 and 6 are composition claims with an intended use. In response to applicant's argument that of Bos et al. have a different intended uses than the instant claims, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Secondly, Bos et al. recite that the pyrimidinyl compounds can be used for a variety of ailments that include headache, especially migraine, (see column 1, lines 29-30).

7. Third, applicants allege that Suto et al. do not suggest the current intended use of the instant claims. In response to applicants' argument that of Suto et al. have a

Art Unit: 1614

different intended uses than the instant claims, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). For these reasons, Suto et al. do teach of pyrimidinyl carboxamide compounds and their pharmaceutical preparations, which render the instant claims obvious to one possessing ordinary skill in the art, (see columns 3-7 and column 10, lines 27-37).

### ***Claim Rejections - 35 USC § 112***

8. The rejection of claims 1, 2, 5 and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of migraine disorders, does not reasonably provide enablement for the broad functional recitation of "disorders responsive to opening of the KCNQ potassium channels" is withdrawn in response to the amendment of November 23, 2003.

9. The rejection of claims 3 and 4 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in response to the amendment of November 23, 2003.

Art Unit: 1614

10. The rejection of claims 2, 4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in response to the amendment of November 23, 2003.

***Claim Rejections - 35 USC § 103***

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1, 2, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bos et al. of U.S. Patent 6,274,588. Bos et al. teach of the pharmaceutical composition of the 4-phenyl-pyrimidine derivatives of formula I, (see column 2, lines 38 and claims 1-10). In fact, these 1,3-diazinyl compounds are known to be useful in treating headaches, especially migraines, (see column 1, lines 29 and 30). Bos et al. teach of the compounds of formula 1, wherein R<sup>5</sup> is lower alkyl, lower alkoxy, amino,

Art Unit: 1614

and phenyl, which correspond to instant variable  $R^2$ . Instant variable of  $R^3$  can be hydrogen as in Bos et al. Instant variable of  $R^1$  can be represented by phenyl as in Bos et al., especially when Bos et al. variable of  $R^1$  is hydrogen,  $n$  is 0, and  $R^2$  is hydrogen. When the variable of  $X$  is  $C(O)NR^4$  and further where  $R^4$  is hydrogen or lower alkyl, this group corresponds to instant variables  $R^4$  or  $R^5$ . In addition, when the Bos et al. variables of  $R^4$  and  $R^4$  are hydrogen and the variable of  $n$  is 0, the instant variables of  $R^4$  and  $R^5$  are clearly rendered obvious. In addition, the selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945). "Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." 325 US at 355, 65 USPQ at 301. See also In re Leshin, 227 F.2d 197, 125 USPQ 416 (CCPA 1960) (selection of a known plastic to make a container of a type made of plastics prior to the invention was held to be obvious). Consequently, it would have been obvious to the skilled artisan to utilize these known 1,3-diazinyl compounds in pharmaceutical compositions regardless of the functional recitations that are instantly incorporated in claims 5 and 6. One having ordinary skill in the art would have been motivated to utilize these known compounds of Bos et al. in any pharmaceutical composition.

14. Claims 1, 2, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suto et al. of U.S. Patent No. 5,811,428. Suto et al. teach of the pyrimidine carboxamide compounds and their analogs as well as their pharmaceutical

Art Unit: 1614

compositions, (see columns 3-8, and from column 10, line 27 to column 11, line 18 and claims 1-27). In addition, the selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945). "Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." 325 US at 355, 65 USPQ at 301. See also In re Leshin, 227 F.2d 197, 125 USPQ 416 (CCPA 1960) (selection of a known plastic to make a container of a type made of plastics prior to the invention was held to be obvious). Consequently, it would have been obvious to the skilled artisan to utilize these known pyrimidine carboxamide compounds and their analogs in pharmaceutical compositions regardless of the functional recitations that are instantly incorporated in claims 5 and 6. One having ordinary skill in the art would have been motivated to utilize these known compounds of Suto et al. in any pharmaceutical composition.

15. Claims 1, 2, 5, and 6 are rejected under 35 U.S.C. 103(a) as being obvious over copending Application No. US 2002/0128277.

16. The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject



Art Unit: 1614

matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(I)(1) and § 706.02(I)(2). Copending Application No. US 2002/0128277 and the instantly claimed application teach of treating migraine disorders with the KCNQ potassium channel opener compounds of 2,4-disubstituted pyrimidine-5-carboxamide derivatives, as does the instant invention. The skilled artisan would have been motivated to select other 2,4-disubstituted pyrimidine-5-carboxamide compounds to treat migraines.

### ***Obviousness-type Double Patenting***

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

Art Unit: 1614

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1, 2, 5, and 6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of copending Application No. US 2002/0128277. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant invention and the copending Application No. US 2002/0128277 teach treating migraine disorders with the KCNQ potassium channel opener compounds of 2,4-disubstituted pyrimidine-5-carboxamide derivatives.

19. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. Claims 1, 2, 5, and 6 are directed to an invention not patentably distinct from claims 1-11 of commonly assigned copending Application No. US 2002/0128277. Specifically, copending Application No. US 2002/0128277 and the instantly claimed application teach of treating migraine disorders with the KCNQ potassium channel opener compounds of 2,4-disubstituted pyrimidine-5-carboxamide derivatives.

21. The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned copending Application No. US 2002/0128277 and the instantly claimed application, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as

prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

22. A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

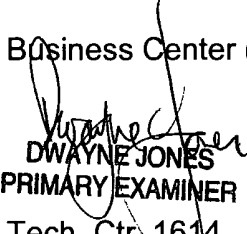
Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (571) 272-0578. The examiner can normally be reached on Mondays, Tuesdays, Thursday, and Fridays from 8:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, may be reached at (571) 272-0584. The official fax No. for correspondence is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Art Unit: 1614

Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see <http://pair-direct.uspto.gov> Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

  
DWAYNE JONES  
PRIMARY EXAMINER

Tech. Ctr. 1614  
April 15, 2004